

WHAT IS CLAIMED IS:

1. A method for evaluating the risk of irinotecan toxicity in a patient comprising
determining the presence of a polymorphism in one or both *UGT1A1* genes of the patient,
5 wherein the polymorphism is in linkage disequilibrium with a *UGT1A1* TA repeat.
2. The method of claim 1, further comprising amplifying from a nucleic acid sample
all or part of 5' flanking region of one or both *UGT1A1* genes to obtain amplification
products and analyzing the amplification products for the presence or absence of a
10 polymorphism.
3. The method of claim 1, wherein the polymorphism is at nucleotide position -3440,
-3401, -3279, -3177, -3175, or -3156 from the *UGT1A1* gene transcriptional start site.
- 15 4. The method of claim 1, wherein the number of TA repeats is 5, 6, 7, or 8 TA
repeats.
5. The method of claim 1, wherein the polymorphism is a -3440C>A polymorphism.
- 20 6. The method of claim 1, wherein the polymorphism is a -3401T>C polymorphism.
7. The method of claim 1, wherein the polymorphism is a -3279G>T polymorphism.
8. The method of claim 1, wherein the polymorphism is a -3177C>G polymorphism.
- 25 9. The method of claim 1, wherein the polymorphism is a -3175A>G polymorphism.
10. The method of claim 1, wherein the polymorphism is a -3156G>A polymorphism.

11. The method of claim 1, wherein determining the presence of a polymorphism in one or both *UGT1A1* genes of the patient comprises determining the nucleotide sequence at position -3156 in one or both genes.

5 12. The method of claim 11, further comprising classifying the UGT1A1 activity level in the patient, whereby identification of a guanine residue indicates the patient does not have a low level of activity.

13. The method of claim 11, further comprising determining the nucleotide sequence
10 at position -3156 of a second *UGT1A1* gene in the patient.

14. The method of claim 11, further comprising administering irinotecan to the patient if a guanine nucleotide is found at position -3516.

15 15. The method of claim 1, further comprising analyzing a glucuronidation rate associated with the polymorphism.

16. The method of claim 1, further comprising optimizing a dose of irinotecan for
administration to the patient.

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17. The method according to claim 1, wherein determining the presence of a polymorphism of a UGT1A1 gene or genes is performed by a hybridization assay.

18. The method according to claim 1, wherein determining the presence of a
25 polymorphism of a UGT1A1 gene or genes is performed by a sequencing or microsequencing assay.

19. The method according to claim 1, wherein determining the presence of a
30 polymorphism of a UGT1A1 gene or genes is performed by an allele-specific amplification assay.

20. The method of claim 1, further comprising administering to the patient irinotecan.

21. The method of claim 20, further comprising administering to the patient a second agent to reduce excretion of an active irinotecan species through the bile.

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22. A method for evaluating the risk of irinotecan toxicity in a patient comprising: determining the nucleotide sequence at position -3156 in one *UGT1A1* gene of the patient.

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23. The method of claim 22, further comprising classifying the UGT1A1 activity level in the patient, whereby identification of a guanine residue indicates the patient does not have a low level of activity.

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24. The method of claim 22, further comprising determining the nucleotide sequence at position -3156 of a second *UGT1A1* gene in the patient.

25. The method of claim 22, further comprising administering irinotecan to the patient if a guanine nucleotide is found at position -3516.

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26. A kit for evaluating the risk of irinotecan toxicity in a patient comprising an oligonucleotide primer to amplify a 5' flanking region of a UGT1A1 gene or genes.

27. The kit of claim 26, further comprising amplification primers of the UGT1A1 gene, wherein the amplification primers amplify haplotype tag SNPs.

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28. The kit of claim 27, wherein the amplification primers amplify a polymorphism at nucleotide position of -3440, -3401, -3279, -3177, -3175, or -3156 from the *UGT1A1* gene transcriptional start site

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29. The kit of claim 27, wherein the amplification primers are comprised in multi-well assay plate.

30. The kit of claim 26, further comprising specific hybridization probes.

31. The kit of claim 30, wherein the specific hybridization probes detect
5 polymorphisms at nucleotide position -3440, -3401, -3279, -3177, -3175, or -3156 from
the *UGT1A1* gene transcriptional start site.

32. The kit of claim 31, wherein the the specific hybridization probes identify
10 whether there is a guanine nucleotide at position -3156 upstream from a *UGT1A1* gene
transcriptional start site.

33. The kit of claim 31, wherein the specific hybridization probes are comprised in an
oligonucleotide array or microarray.

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